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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/786,503	06/07/2001	Hiroshi Oda	11283-009001	1563

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EXAMINER	
COUNTS, GARY W	
ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 07/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/786,503	ODA ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21 and 37-43* is/are pending in the application.

4a) Of the above claim(s) *37-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21 and 41-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

The amendment filed May 3, 2004 is acknowledged and has been entered.

Election/Restrictions

1. Newly submitted claims 37-40 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Claim 37 claims a method of detection of an early-stage renal disease . The method or claim 37 requires the sample be a blood sample and the claimed invention in claim 21 does not require this limitation, but rather requires the sample to be a urine sample. Also, the method of claim 37 requires the concentration of creatinine in the serum of the test subject being normal and the claimed invention in claim 21 does not require this limitation.

Claim 38 claims a method of detection of an early-stage renal disease. The method of claim 38 requires the sample to be a blood sample and the claimed invention in claim 21 does not require this limitation, but rather requires the sample to be a urine sample. Also, the method of claim 38 requires that the test subject does not exhibit proteinura and the claimed invention in claim 21 does not require this limitation. Claim 38 also requires a reference blood sample and claim 21 does not require this limitation.

Claim 39 claims a method of detection of an early-stage renal disease. The method of claim 39 requires the sample to be a blood sample and the claimed invention in claim 21 does not require this limitation, but rather requires the sample to be a urine sample. Also, the method of claim 39 requires the concentration of albumin in the urine

of the test subject be normal and the claimed invention in claim 21 does not require this limitation.

Claim 40 claims a method of detection of an early-stage renal disease. The method of claim 40 requires the sample to be a blood sample and the claimed invention in claim 21 does not require this limitation, but rather requires the sample to be a urine sample. Also, the method of claim 40 requires the concentration of creatinine in the serum of the test subject being normal; the concentration of albumin in the urine of the test subject being normal and the test subject not exhibiting proteinuria and the claimed invention in claim 21 does not require this limitation.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 37-40 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 41 and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 41, line 2 the recitation "a body fluid sample" is vague and indefinite. It is unclear if applicant is referring to the urine sample in claim 21 or if applicant is referring to another body fluid. Please clarify.

Claim 43 is vague and indefinite because claim 43 contradicts claim 21. Claim 21 requires that the reference value of human L-PGDS concentration is from urine. However, claim 43 requires that the reference value of human L-PGDS concentration is obtained from blood samples. Does the blood sample reference value replace the urine reference value or are both the blood sample reference value and the urine sample reference value somehow used together as an indication that the test subject has early stage renal disease.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 21, 41 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoffman et al (Molecular characterization of beta-trace protein in human serum and urine: a potential diagnostic marker for renal disease, Gylcobiology, vol 7, no 4 p 499-506 (1997)).

Hoffman et al disclose that beta-trace protein (lipocalin-type prostaglandin D synthase (L-PGDS)) was isolated from cerebrospinal fluid, serum, plasma and urine samples of normal volunteers and sera and hemofiltrate of patients with chronic renal failure (abstract). Hoffman et al disclose that serum L-PGDS concentration in patients with end-stage renal failure increased as compared to the L-PGDS of the normal volunteers. Hoffman et al disclose that serum beta-trace (L-PGDS) concentrations were determined by quantitative immunoaffinity chromatography in conjunction with amino acid sequencing and SDS gel electrophoresis and revealed a broad range of concentrations (p. 504, col 2, lines 36-60).

Even though Hoffman et al is silent on a method of detection of an early-stage renal disease, Hoffman et al teaches that beta-trace protein (L-PGDS) accumulates more significantly in serum in pathological conditions than other proteins in current use and that the beta-trace protein may be used for the study and early diagnosis of renal diseases (p. 505, lines 14-21). Therefore, it would have been obvious to one of ordinary skill in the art to have a reasonable expectation of success to use the method of Hoffman et al for the detection of early-stage renal disease.

With respect to a urine sample as recited in the instant claims. Hoffman et al disclose that the proteins of urinary and serum-derived beta-trace proteins are identical (p. 501 and 504) and Hoffman et al further teaches the detection of beta-trace proteins in urine. Therefore, it would have been obvious to one of ordinary skill in the art to use urine as the sample for beta-trace proteins.

Response to Arguments

8. Applicant's arguments filed May 3, 2004 have been fully considered but they are not persuasive.

Applicant argues that elevation of the level of a biological molecule (e.g., L-PGDS) in a first body fluid (e.g., urine) in a pathological condition of interest (e.g., renal failure) cannot be predicted by the mere fact of an elevated level of the same biological molecule in a second body fluid (e.g., blood). Applicant states that one of skill in the art would readily envisage circumstances under which the relative levels of a biological molecule in two bodily fluids either would not be correlated or would be negatively correlated. Applicant directs Examiner's attention to an article published after the

priority date of the instant application (Hirawa et al, Nephron 87: 321-327, 2001). Applicant states that this article reported there is no relationship between plasma L-PGDS concentration and the level of urinary L-PGDS (applicant directed Examiner's attention to the abstract). This is not found persuasive because it is unclear what relationship Applicant is referring to. Further, it appears that there is a relationship in that L-PGDS levels are increased in both serum and urine levels as compared to healthy patients and that urine has even higher levels of L-PGDS in renal failure. Also, it is not found persuasive because Hoffman et al teach that L-PGDS can be found in both serum and urine sample and that the proteins are identical. Hoffman specifically teaches that in renal diseases that the elimination of proteins through the kidney is disturbed resulting in elevated concentrations of proteins and since Hoffman et al teaches higher levels of L-PGDS in renal failure patients and specifically teaches that this protein is identical in serum and urine, it would have been obvious to one of ordinary skill in the art to use a urine sample as the sample for beta-trace proteins. Hoffman et al also teaches that proteins are elevated in renal disease, and that L-PDGS may be used for the study and early diagnosis of renal diseases. Therefore, one of ordinary skill in the art would expect increased levels of L-PGDS in the urine of renal disease patients and one of ordinary skill in the art would have a reasonable expectation of success to use urine as a sample and use the method of Hoffman et al for the detection of early-stage renal disease.

With respect to the arguments directed toward claims 37-40, the arguments are moot because claims 37-40 have been withdrawn from consideration as being directed to a non-elected invention.

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary W. Counts
Examiner
Art Unit 1641
June 30, 2004

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SUPERVISORY PATENT EXAMINER
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07/07/04